10/961 231

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=> d his

     (FILE 'HOME' ENTERED AT 13:13:18 ON 18 JUL 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:13:51 ON 18 JUL 2006
L1           292 S "GANP"
L2            82 S (MOUSE OR MURINE) AND L1
L3       7791094 S CLON? OR EXPRESS? OR RECOMBINANT
L4            70 S L2 AND L3
L5            22 DUP REM L4 (48 DUPLICATES REMOVED)
                 E SAKAGUCHI N/AU
L6           848 S E3-E5
                 E KUWAHARA K/AU
L7           893 S E3
L8          1637 S L6 OR L7
L9            51 S L1 AND L8
L10           25 DUP REM L9 (26 DUPLICATES REMOVED)
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 NEWS  7  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 07   Coverage of Research Disclosure reinstated in DWPI
 NEWS 14  JUl 11   CHEMSAFE reloaded and enhanced
 NEWS 15  JUl 14   FSTA enhanced with Japanese patents

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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FILE 'HOME' ENTERED AT 13:13:18 ON 18 JUL 2006

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
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FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:13:51 ON 18 JUL 2006
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FILE 'EMBASE' ENTERED AT 13:13:51 ON 18 JUL 2006

FILE 'BIOSIS' ENTERED AT 13:13:51 ON 18 JUL 2006

FILE 'BIOTECHDS' ENTERED AT 13:13:51 ON 18 JUL 2006

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FILE 'NTIS' ENTERED AT 13:13:51 ON 18 JUL 2006

FILE 'LIFESCI' ENTERED AT 13:13:51 ON 18 JUL 2006


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=> s "GANP"
L1          292 "GANP"

=> s mouse or murine
<------User Break------>

=> s (mouse or murine) and l1
L2           82 (MOUSE OR MURINE) AND L1

=> s clon? or express? or recombinant
L3      7791094 CLON? OR EXPRESS? OR RECOMBINANT

=> s l2 and l3
L4           70 L2 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           22 DUP REM L4 (48 DUPLICATES REMOVED)

=> d 1-22 ibib ab

L5   ANSWER 1 OF 22     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2005341448     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15994971
TITLE:              Increased expression of germinal
                    center-associated nuclear protein RNA-primase is associated
                    with lymphomagenesis.
AUTHOR:             Fujimura Satoru; Xing Yan; Takeya Motohiro; Yamashita
                    Yasuyuki; Ohshima Koichi; Kuwahara Kazuhiko; Sakaguchi
                    Nobuo
CORPORATE SOURCE:   Department of Immunology, Graduate School of Medical
                    Sciences, Kumamoto University, Honjo, Kumamoto, Japan.
SOURCE:             Cancer research, (2005 Jul 1) Vol. 65, No. 13, pp. 5925-34.
                    Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
```

ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 6 Jul 2005
Last Updated on STN: 8 Sep 2005
Entered Medline: 7 Sep 2005

AB Lymphomas arise containing abnormalities of various differentiation stage-specific molecules. In the study reported here, we have shown abnormal up-regulation of germinal center B cell-associated GANP in various human lymphomas including mantle cell, diffuse large B cell, and Hodgkin lymphoma, by immunohistochemical analysis. To study the role of GANP in lymphomagenesis, we generated mutant mice (ganp-Tg) that express the transgenic ganp gene under immunoglobulin enhancer and promoter control. Ganp-Tg mice showed a high incidence of lymphomagenesis (29.5%) after aging with a non-B/non-T cell surface phenotype having slight CD45R/B220 expression and Ig transcripts of rearranged VH-DH-JH IgH loci. Lymphomas generated in ganp-Tg mice displayed similar pathologic characteristics to mouse reticulum cell neoplasm or Hodgkin lymphoma-like lesions. The VH sequences of individual mice showed that the tumors proliferated from a single clone or oligoclones, as is found in human diffuse large B-cell lymphomas and Hodgkin lymphoma. These results suggest that GANP overexpression is a causative factor in the generation of B lymphomas.

L5 ANSWER 2 OF 22 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005560234 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16237049
TITLE: Cutting edge: double-stranded DNA breaks in the IgV region gene were detected at lower frequency in affinity-maturation impeded GANP-/- mice
AUTHOR: Kawatani Yousuke; Igarashi Hideya; Matsui Takeshi; Kuwahara Kazuhiko; Fujimura Satoru; Okamoto Nobukazu; Takagi Katsumasa; Sakaguchi Nobuo
CORPORATE SOURCE: Department of Immunology, Graduate School of Medicine, Kumamoto University, Japan.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2005 Nov 1) Vol. 175, No. 9, pp. 5615-8.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 21 Oct 2005
Last Updated on STN: 16 Dec 2005
Entered Medline: 29 Nov 2005

AB Double-stranded DNA breaks (DSBs) at the IgV region (IgV) genes might be involved in somatic hypermutation and affinity-maturation of the B cell receptor in response to T cell-dependent Ag. By ligation-mediated PCR, we studied IgV DSBs that occurred in mature germinal center B cells in response to nitrophenyl-chicken gamma-globulin in a RAG1-independent, Ag-dependent, and IgV-selective manner. We quantified their levels in GANP-deficient B cells that have impaired generation of high-affinity Ab. GANP-/- B cells showed a decreased level of DSBs with blunt ends than control B cells and, on the contrary, the ganp gene transgenic (GANPTg) B cells showed an increased level. These results suggested that the level of IgV DSBs in germinal center B cells is associated with GANP expression, which is presumably required for B cell receptor affinity maturation.

L5 ANSWER 3 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:257246 BIOSIS
DOCUMENT NUMBER: PREV200510047440
TITLE: Generation of high-affinity antibody against T

cell-dependent antigen in the Ganp gene-transgenic mouse.

AUTHOR(S): Sakaguchi, Nobuo [Reprint Author]; Kimura, Tetsuya; Matsushita, Shuzo; Fujimura, Satoru; Shibata, Junji; Araki, Masatake; Sakamoto, Tamami; Minoda, Chiemi; Kuwahara, Kazuhiko

CORPORATE SOURCE: Kumamoto Univ, Grad Sch Med Sci, Dept Immunol, 1-1-1,Honjo, Kumamoto 8608556, Japan
nobusaka@kaiju.medic.kumamoto-u.ac.jp

SOURCE: Journal of Immunology, (APR 15 2005) Vol. 174, No. 8, pp. 4485-4494.
CODEN: JOIMA3. ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005

AB Generation of high-affinity Ab is impaired in mice lacking germinal center-associated DNA primase (GANP) in B cells. In this study, we examined the effect of its overexpression in ganp transgenic C57BL/6 mice (Ganp(Tg)). Ganp (Tg) displayed normal phenotype in B cell development, serum Ig levels, and responses against T cell-independent Ag; however, it generated the Ab with much higher affinity against nitrophenyl-chicken gammaglobulin in comparison with C57BL/6. To further examine the affinity increase, we established hybridomas producing high-affinity mAbs and compared their affinities using BIAcore. C57BL/6 generated high-affinity anti-nitrophenyl mAbs (K-D similar to 2.50 X 10(-7) M) of IgG1/lambda 1 and contained the V(H)186.2 region with W33L mutation. GanpTg generated much higher affinity (K-D > 1.57 X 10(-9) M) by usage of V(H)186.2 as well as noncanonical V(H)7183 regions. Ganp(Tg) also generated exceptionally high-affinity anti-HIV-1 (V3 peptide) mAbs (K, > 9.90 x 10-11 m) with neutralizing activity. These results demonstrated that GANP is involved in V region alteration generating high-affinity Ab.

L5 ANSWER 4 OF 22 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2005478431 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16129705

TITLE: Protein phosphatase subunit G5PR is needed for inhibition of B cell receptor-induced apoptosis.

AUTHOR: Xing Yan; Igarashi Hideya; Wang Xiaodan; Sakaguchi Nobuo

CORPORATE SOURCE: Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, Japan.

SOURCE: The Journal of experimental medicine, (2005 Sep 5) Vol. 202, No. 5, pp. 707-19. Electronic Publication: 2005-08-29.
Journal code: 2985109R. ISSN: 0022-1007.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200602

ENTRY DATE: Entered STN: 9 Sep 2005
Last Updated on STN: 28 Feb 2006
Entered Medline: 27 Feb 2006

AB B cell receptor (BCR) cross-linking induces B cell proliferation and sustains survival through the phosphorylation-dependent signals. We report that a loss of the protein phosphatase component G5PR increased the activation-induced cell death (AICD) and thus impaired B cell survival. G5PR associates with GANP, whose expression is up-regulated in mature B cells of the peripheral lymphoid organs. To study G5PR function, the G5pr gene was conditionally targeted with the CD19-Cre combination (G5pr(-/-) mice). The G5pr(-/-) mice had a decreased number of splenic B cells (60% of the

controls). G5pr(-/-) B cells showed a normal proliferative response to lipopolysaccharide or anti-CD40 antibody stimulation but not to BCR cross-linking with or without IL-4 in vitro. G5pr(-/-) B cells did not show abnormalities in the BCR-mediated activation of Erks and NF-kappaB, cyclin D2 induction, or Akt activation. However, G5pr(-/-) B cells were sensitive to AICD caused by BCR cross-linking. This was associated with an increased depolarization of the mitochondrial membrane and the enhanced activation of c-Jun NH(2)-terminal protein kinase and Bim. These results suggest that G5PR is required for the BCR-mediated proliferation associated with the prevention of AICD in mature B cells.

L5 ANSWER 5 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 4
ACCESSION NUMBER: 2004-15238 BIOTECHDS
TITLE: Transgenic mammals carrying GANP for production of high-affinity antibodies, used as diagnostics and remedies for various diseases e.g. hepatitis C, adult T-cell leukemia, AIDS and mad-cow disease;
plasmid-mediated gene transfer and expression in B-lymphocyte for transplantation in transgenic mouse for recombinant antibody production for use in disease diagnosis
AUTHOR: SAKAGUCHI N
PATENT ASSIGNEE: KUMAMOTO TECHNOLOGY and IND FOUND
PATENT INFO: WO 2004040969 21 May 2004
APPLICATION INFO: WO 2002-JP11598 7 Nov 2002
PRIORITY INFO: WO 2002-11598 7 Nov 2002; WO 2002-11598 7 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2004-400492 [37]
AB DERWENT ABSTRACT:
NOVELTY - A transgenic mammal is transferred with GANP (undefined) gene, its descendants, or a part of them.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a method for producing a high-affinity antibody by administering an antigen to the transgenic mammal or its descendants prior to obtaining such antibody; (2) a high- affinity antibody or its fragment thus produced; and diagnostics, preventives or remedies for diseases containing the antibodies or their fragments; (3) a human- type antibody or its fragment containing the V region of a high-affinity antibody; (4) remedies containing such human-type antibody; and (5) high-affinity antibody-producing cells collected from the transgenic mammals or their descendants after administering an antigen.
ACTIVITY - Virucide; Cytostatic; Anti-HIV; Neuroprotective. No biological data given.
MECHANISM OF ACTION - None given.
USE - The produced antibodies are useful as diagnostics and remedies for various diseases e.g. hepatitis C, adult T-cell leukemia, AIDS and mad-cow disease.
ADMINISTRATION - Administration of the remedies is oral or non-oral, e.g. at 10 mug/kg to 1000 mg/kg.
ADVANTAGE - Such produced high-affinity antibody is efficacious as diagnostic or remedy.
EXAMPLE - Transgenic mice were obtained after transferring with a mouse GANP gene-containing pLG vector. After administering e.g. trinitrophenyl-keyhole limpet hemocyanin (TNP-KLH) as antigen, the antigen-specific antibody production was verified. (73 pages)

L5 ANSWER 6 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 5
ACCESSION NUMBER: 2004-12391 BIOTECHDS
TITLE: New G5PR protein having avidity with respect to germinal center-associated nuclear protein (GANP), useful in

diagnosing cancer or autoimmune disease e.g., systemic lupus erythematosus;
recombinant protein production via plasmid expression in host cell for use in disease diagnosis

PATENT ASSIGNEE: ZH KUMAMOTO TECHNO SANGYO ZAIDAN
PATENT INFO: JP 2004073142 11 Mar 2004
APPLICATION INFO: JP 2002-241342 22 Aug 2002
PRIORITY INFO: JP 2002-241342 22 Aug 2002; JP 2002-241342 22 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2004-220136 [21]

AB DERWENT ABSTRACT:

NOVELTY - A G5PR protein (I) having avidity with respect to GANP protein, and comprising a fully defined sequence (S1) of 453 amino acids as given in the specification or a sequence which has deletion, substitution and/or insertion in amino acid(s) of (S1) or a sequence which has 60% or more homology with (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a protein composite (II) containing (I) and protein phosphatase; (2) a gene (III) encoding (I); (3) a vector (IV) containing (III); (4) a transformed cell containing (III) or (IV); (5) an antibody (V) with respect to (I) or (II); (6) a reagent (VI) for a GANP binding protein measurement, containing (V); and (7) a kit (VII) for a GANP binding protein measurement, containing (V).

BIOTECHNOLOGY - Preferred Protein Composite: In (II), the protein phosphatase is the protein phosphatase 5 (PP5) or protein phosphatase 2A (PP2A). Preferred Gene: (III) has a fully defined sequence (S2) of 1575 nucleotides as given in the specification or a sequence which has deletion, addition or substitution in nucleotide(s) of (S2) or a sequence which hybridizes under stringent conditions with (S2).

USE - (VI) or (VII) is useful for a diagnosis of cancer or an autoimmune disease (claimed). (I) detection in the sample is useful in diagnosing cancer such as endometrium cancer, endometrium tumor, breast cancer, colon cancer, prostatic cancer, lung cancer, renal cancer, neuroblastoma, bladder cancer, melanoma and autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, rheumatic fever, tuberosity frequent occurrence arteritis, Behcet's disease, scleroderma, Sjogren's syndrome, chronic thyroiditis and osteomalacia.

ADVANTAGE - (VI) or (VII) is efficient in identifying cancer or autoimmune disease.

EXAMPLE - A full length G5PR cDNA of mouse was isolated by rapid amplification of cDNA ends (RACE) method. On sequencing the G5PR gene had a fully defined sequence of 1575 nucleotides as given in the specification and encoded G5PR protein had a fully defined sequence of 453 amino acids as given in the specification. Myc label sequence ggaagcttgccaccatggagcagaaactcatctctgaagaggatctggtacccc was introduced into pcDNA3.1/HisA vector to produced pcDNA-Myc construct. The GFP (green fluorescent protein) gene from pEGFP was inserted into the obtained pcDNA-Myc construct to produce pcDNA-Myc-EGFP. The obtained mouse G5PR cDNA was introduced into pcDNA-Myc-EGFP and Myc-EGFP-G5PR fragment was reintroduced into pCXN2 to produce pCXN2-Myc-G5PR. COS-7 cell cultured in Dulbecco-modified eagle culture medium was transfected with pCXN2-Myc-G5PR and flag-GANP. Then transfected cell was collected and incubated with 4 microliters of anti-Myc9E10 monoclonal-antibody or 4 microliters of anti-flag M2 monoclonal antibody for 1 hour. After incubation, the immunoprecipitation of Myc-EGFP-G5PR or Myc-EGFP (control) was analyzed. On analysis, Myc-EGFP-G5PR co-precipitated flag-GANP while co-precipitation was not observed by Myc-EGFP. Thus G5PR had high efficiency in coupling with GANP in a mammalian cell.(31 pages)

L5 ANSWER 7 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2004-15408 BIOTECHDS
TITLE: Transgenic mammal transformed with germinal center associated nuclear protein (GANP) gene for production of high-affinity antibodies as diagnostic reagents and disease therapy;
involving vector plasmid pLG-mediated gene transfer and expression in host cell for use in therapy
AUTHOR: SAKAGUCHI N
PATENT ASSIGNEE: IMMUNOKICK INC
PATENT INFO: WO 2004040971 21 May 2004
APPLICATION INFO: WO 2003-JP14221 7 Nov 2003
PRIORITY INFO: WO 2002-11598 7 Nov 2002; WO 2002-11598 7 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2004-411378 [38]
AB DERWENT ABSTRACT:
NOVELTY - Transgenic non-human animals and their offspring are new which are transformed with germinal center associated nuclear protein (GANP) gene.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) tissues and organs of the transgenic mammals; (2) preparation of high-affinity antibodies by immunizing the transgenic animals with an antigen; (3) high-affinity antibodies and their fragments obtained by the method; (4) high-affinity antibody secreting cells produced using the method; and (5) drug compositions containing the high-affinity antibodies or their fragments.

BIOTECHNOLOGY - Preferred Mammal: mouse. Preferred antibodies: polyclonal or monoclonal with neutralizing activity at below 10-7M. The antibodies include human or humanized antibodies or their fragments containing V regions from the antibodies prepared using the transgenic animals.

ACTIVITY - Virucide. No suitable data given.

MECHANISM OF ACTION - Viral antigen inhibitor.

USE - Production of high-affinity antibodies to viral antigens for treatment and prevention of infection by viruses such as human immunodeficiency virus and hepatitis C virus.

ADMINISTRATION - Antibody is administered at 1 microgram to 100 mg (preferably 50 microgram to 50 mg) per kilo body weight per day subcutaneous, transdermal, intravenous, intramuscular or intraperitoneal.

EXAMPLE - GANP gene (WO2000/50611) is inserted into pLG vector (a vector containing the enhancer region from human immunoglobulin gene) and used to transform fertilized ova of C57BL/6 mice by microinjection. The transformed ova are implanted and brought to term to give transgenic mice. RT-PCR on total RNA isolated from spleen B cells from these mice shows that GANP has higher expression in these transgenic mice than in wild-type mice. The mice are immunized using 100 microgram of p-nitrophenyl derivatized chicken gamma-globulin (NP-CG). Spleen cells from immunized mice are fused with P3U1 myeloma cells and the hybridomas obtained are screened for anti-NP-CG activity. Supernatant from a culture of positive clone is subjected to ELISA assay using immobilized NP2-BSA or NP17-BSA antigen (bovine serum albumin containing 2 or 17 p-nitrophenyl groups per albumin molecule) and peroxidase-labelled anti-mouse IgG. The ratio of binding to NP2-BSA to that to NP17-BSA is calculated as a measure of neutralizing ability. A similar experiment is conducted using wild-type c57BL/6 mice. The binding ratio for wild-type mice is 30% and for transgenic mice is higher, one hybridoma clone (G2-9) having a binding ratio of 80%.(214 pages)

L5 ANSWER 8 OF 22 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004147002 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15034025
TITLE: Microarray analysis of Lyn-deficient B cells reveals

germinal center-associated nuclear protein and other genes associated with the lymphoid germinal center.

AUTHOR: Mirnics Zeljka Korade; Caudell Eva; Gao YanHua; Kuwahara Kazuhiko; Sakaguchi Nobuo; Kurosaki Tomohiro; Burnside Joan; Mirnics Karoly; Corey Seth J

CORPORATE SOURCE: Department of Pediatrics, University of Pittsburgh, School of Medicine, Children's Hospital of Pittsburgh, Pittsburgh, PA 15213, USA.

CONTRACT NUMBER: K02HL03794 (NHLBI)
R21MH/NS62760-01 (NIMH)
R29CA74422 (NCI)

SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Apr 1) Vol. 172, No. 7, pp. 4133-41.
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200407

ENTRY DATE: Entered STN: 26 Mar 2004
Last Updated on STN: 1 Aug 2004
Entered Medline: 30 Jul 2004

AB Lyn is the only member of the Src family expressed in DT40 B cells, which provide a unique model to study the singular contribution of this protein tyrosine kinase (PTK) family to cell signaling. In these cells, gene ablation of Lyn leads to defective B cell receptor signaling. Complementary DNA array analysis of Lyn-deficient DT40 cells shows that the absence of Lyn leads to down-regulation of numerous genes encoding proteins involved in B cell receptor signaling, proliferation, control of transcription, immunity/inflammation response, and cytoskeletal organization. Most of these expression changes have not been previously associated with Lyn PTK signaling. They include alterations in mRNA levels of germinal center-associated nuclear protein (germinal center-associated DNA primase) (GANP), CD74, CD22, NF-kappaB, elongation factor 1alpha, CD79b, octamer binding factor 1, Ig H chain, stathmin, and gamma-actin. Changes in GANP expression were also confirmed in Lyn-deficient mice, suggesting that Lyn PTK has a unique function not compensated for by other Src kinases. Because Lyn-deficient mice have impaired development of germinal centers in spleen, the decreased expression of GANP in the Lyn-deficient DT40 cell line and Lyn-deficient mice suggests that Lyn controls the formation and proliferation of germinal centers via GANP. GANP promoter activity was higher in wild-type vs Lyn-deficient cells. Mutation of the PU.1 binding site reduced activity in wild-type cells and had no effect in Lyn-deficient cells. The presence of Lyn enhanced PU.1 expression in a Northern blot. Thus, the following new signaling pathway has been described: Lyn-->PU.1--> GANP.

L5 ANSWER 9 OF 22 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:151766 SCISEARCH

THE GENUINE ARTICLE: 768FU

TITLE: Germinal center-associated nuclear protein contributes to affinity maturation of B cell antigen receptor in T cell-dependent responses

AUTHOR: Kuwahara K; Fujimura S; Takashi Y; Nakagata N; Takemori T; Aizawa S; Sakaguchi N (Reprint)

CORPORATE SOURCE: Kumamoto Univ, Grad Sch Med Sci, Dept Immunol, Kumamoto 8608556, Japan (Reprint); Natl Inst Infect Dis, Dept Immunol, Shinjuku Ku, Tokyo 1628640, Japan; Kumamoto Univ, Ctr Anim Resources & Dev, Div Reprod Engn, Kumamoto 8600811, Japan; RIKEN, Ctr Dev Biol, Lab Vertebrate Body Plan, Chuo Ku, Kobe, Hyogo 6500047, Japan; PRESTO,

Kawaguchi, Saitama 3320012, Japan; CREST, Japan Sci & Technol Agcy, Kawaguchi, Saitama 3320012, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (27 JAN 2004) Vol. 101, No. 4, pp. 1010-1015.
ISSN: 0027-8424.
PUBLISHER: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Acquired immunity depends on proliferation and differentiation of antigen (Ag)-specific B cells in germinal centers (GCs) of lymphoid follicles in response to T cell-dependent Ags. Here, we studied the function of GC-associated nuclear protein that is selectively up-regulated in GC-B cells. B cell-specific ganp-deficient mice were compromised in affinity maturation of hapten-specific antibodies against T cell-dependent Ags with retarded development of GCs. B cell numbers and development, serum Ig levels, mitogen-induced B cell proliferation in vitro, and responses to T cell-independent Ag were nearly normal; however, the mutant B cells showed a decrease in anti-CD40-induced proliferation and an increased susceptibility to B cell apoptosis in vitro and in vivo. B cell-specific ganp-deficient mice showed a decreased frequency of variable-region somatic mutations, especially of the high-affinity type (W-33 --> L) in the V(H)186.2 region against nitrophenyl-chicken gamma globulin, whereas the class switching was normal. We conclude that GC-associated nuclear protein is necessary for generation or maintenance of 13 cells with high-affinity B cell Ag receptors during the maturation in GCs.

L5 ANSWER 10 OF 22 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:332078 SCISEARCH
THE GENUINE ARTICLE: 808FM
TITLE: The germinal center response
AUTHOR: Wolniak K L; Shinall S M; Waldschmidt T J (Reprint)
CORPORATE SOURCE: Univ Iowa, Coll Med, Dept Pathol, Interdisciplinary Immunol Program, Iowa City, IA 52242 USA (Reprint); Univ Iowa, Coll Med, Med Scientist Training Program, Iowa City, IA 52242 USA
COUNTRY OF AUTHOR: USA
SOURCE: CRITICAL REVIEWS IN IMMUNOLOGY, (2004) Vol. 24, No. 1, pp. 39-65.
ISSN: 1040-8401.
PUBLISHER: BEGELL HOUSE INC, 145 MADISON AVE, NEW YORK, NY 10016 USA.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 199
ENTRY DATE: Entered STN: 23 Apr 2004
Last Updated on STN: 23 Apr 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The, germinal center reaction is the foundation of T-cell-dependent humoral responses. Antigen-specific B cells recruited into germinal centers undergo a complex cellular program that allows for extensive expansion, isotype switching, somatic hypermutation, and differentiation into antibody-forming cells and memory cells. Importantly, the germinal center environment filters the repertoire of differentiating B cells such that high affinity variants are preferentially selected while low affinity or self-reactive clones are eliminated by apoptosis. The present article reviews-the many processes that govern germinal center

B-cell differentiation, as well as the cellular and molecular elements necessary to initiate and sustain a germinal center response. The major histologic features of the germinal center are also discussed, as well as the current dominant models of the germinal center reaction in humans and mice. Finally, a new model of murine B-cell differentiation is described on the basis of a multiparameter flow cytometric kinetic analysis of germinal center B-cells.

L5 ANSWER 11 OF 22 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003265520 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12791315
TITLE: Spontaneous increase of plasma-like cells with high GANP expression in the extrafollicular region of lymphoid organs of autoimmune-prone mice
AUTHOR: Fujimura Satoru; Kuwahara Kazuhiko; Ezaki Taichi; Tomita Kimio; Hirose Sachiko; Sakaguchi Nobuo
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto 860-0811, Japan.
SOURCE: Journal of autoimmunity, (2003 Jun) Vol. 20, No. 4, pp. 291-301.
Journal code: 8812164. ISSN: 0896-8411.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 8 Jun 2003
Last Updated on STN: 2 Mar 2004
Entered Medline: 26 Feb 2004

AB Autoimmune-prone mice bear a hyper-active B cell population generated spontaneously in peripheral lymphoid organs. Expression of beta RNA-primase GANP was shown to be an activation marker in lymphoid follicle germinal center (GC) B cells after immunization with T cell-dependent antigen (TD-Ag) in normal mice. In this study, we examined the expression of GANP in lymphoid tissues of autoimmune-prone mice. GANP expression was up-regulated in GC-B cells after stimulation with TD-Ags; however, highly GANP-positive (GANP(hi)) cells were also observed in lymph nodes of non-immunized MRL/lpr mice. GANP(hi)cells in lymph nodes as well as in spleens of the different autoimmune-prone strains, MRL/lpr, NZB, (NZBxNZW)F1 and BXSB, gradually increased with age. This population was detected only in small numbers in the red pulp region of the spleen after immunization with TD-Ag in normal C57BL/6 and BALB/c mice. GANP(hi)cells had a B220(-)IgM(+)Syndecan-1(+)phenotype, but were negative for PAS-staining and bromo-deoxyuridine incorporation. These results demonstrate that GANP(hi)plasma-like cells appear in lymph nodes of autoimmune mice during aging, suggesting that the new plasma cell population might be generated after hyper-activation of B cells during the course of autoimmune disease.

L5 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:937303 HCAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2002355079	A2	20021210	JP 2002-69354		20020313
PRIORITY APPLN. INFO.:			JP 2001-73183	A	20010314
			JP 2001-74993	A	20010315
			JP 2001-102519	A	20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L5 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:917171 HCAPLUS
DOCUMENT NUMBER: 138:13211
TITLE: Role of GANP in B cell activation
AUTHOR(S): Kuwahara, Kazuhiko; Sakaguchi, Nobuo
CORPORATE SOURCE: Sch. Med., Kumamoto Univ., Japan
SOURCE: Tanpakushitsu Kakusan Koso (2002), 47(16, Zokango), 2300-2305
CODEN: TAKKAJ; ISSN: 0039-9450
PUBLISHER: Kyoritsu Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on roles of nuclear factor GANP with DNA primase activity in B cell proliferation and activation in the germinal center (GC), discussing isolation and structure of GANP mol., MCM (minichromosome maintenance) complex contg DNA helicase activity, binding of GANP with MCM3, role of GANP as a novel DNA primase in GC-B cell proliferation, mol. mechanism inducing GANP expression in relation to B cell differentiation, and establishment of ganp-deficient mice aiming at in vivo functional anal. of GANP.

L5 ANSWER 14 OF 22 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002457721 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12167160
TITLE: MCM3-binding GANP DNA-primase is associated with a novel phosphatase component G5PR.
AUTHOR: Kono Yoshihiko; Maeda Kazuhiko; Kuwahara Kazuhiko; Yamamoto Hideyuki; Miyamoto Eishichi; Yonezawa Kazuyoshi; Takagi Katsumasa; Sakaguchi Nobuo
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto, 860-0811, Japan.
SOURCE: Genes to cells : devoted to molecular & cellular mechanisms, (2002 Aug) Vol. 7, No. 8, pp. 821-34.
Journal code: 9607379. ISSN: 1356-9597.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 10 Sep 2002
Last Updated on STN: 26 Mar 2003
Entered Medline: 25 Mar 2003

AB BACKGROUND: GANP, carrying DNA-primase and MCM3-binding domains, is up-regulated in germinal centre B cells. To understand the regulatory function of GANP upon MCM complex, we searched for GANP -associated molecules by yeast two-hybrid screening. RESULTS: Using the 1 kb fragment (G5) of the ganp cDNA, we identified a clone named G5PR that is structurally homologous to known regulatory subunits of protein phosphatases (PPases) and determined the association of G5PR with GANP in vivo in the DNA transfectant. G5PR is associated with protein phosphatase 5 (PP5) through its tetratricopeptide-repeat (TPR) domain. Pull-down assays demonstrated that G5PR is also associated with protein phosphatase 2A (PP2A), the complex of A subunit (PR65) and the catalytic (C) subunit (PP2Ac), similar to the B" subunit. The G5PR-associated complex had phosphatase activity on casein, histone H1 and MCM3 in vitro, but the addition of G5PR did not stimulate or inhibit the phosphatase activities of PP5 and PP2A. The cellular localization of G5PR in transfected cells varies during cell cycling, appearing in the nucleus during prophase, in the peri-chromatin during mitotic phase, and in the cytoplasm after cell division. CONCLUSION: G5PR is capable of recruiting two kinds of PPases, PP5 and PP2A, into the GANP/MCM3 complex, which might regulate its phosphorylation state during cell cycle progression.

L5 ANSWER 15 OF 22 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003352481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12885157
TITLE: Involvement of GANP in B cell activation in T cell-dependent antigen response.
AUTHOR: Sakaguchi Nobuo; Fujimura Satoru; Kuwahara Kazuhiko
CORPORATE SOURCE: Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto 860-0811, Japan.. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Developmental immunology, (2002 Sep) Vol. 9, No. 3, pp. 169-72.
Journal code: 9200624. ISSN: 1044-6672.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 30 Jul 2003
Last Updated on STN: 17 Sep 2003
Entered Medline: 16 Sep 2003

AB Adaptive immunity is dependent on proliferation of antigen-driven B cells for clonal expansion in germinal centers (GCs) against T cell-dependent antigens (TD-Ag), accompanied with somatic hypermutation of variable-region gene and class switching of B cell antigen receptors. To study molecular mechanisms for B cell differentiation in GCs, we have identified and studied a 210kDa GANP protein expressed in GC-B cells. GANP has domains for MCM3-binding and RNA-primase activities and is selectively up-regulated in centrocytes surrounded with follicular dendritic cells (FDCs) upon immunization with TD-Ag in vivo and in B cells stimulated with anti-CD40 monoclonal antibody in vitro, which suggested that GANP plays a certain important role in the maturation of immunoglobulin or selection of B cells in GC during the immune response to TD-Ag. Since this up-regulation has not been detected in T cells in GCs and in Concanavalin A-stimulated T cells in vitro, selective function of GANP molecule on B cell proliferation and differentiation might exist.

L5 ANSWER 16 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:356436 BIOSIS
DOCUMENT NUMBER: PREV200300356436
TITLE: Microarray Analysis of Lyn-Deficient B Cells Reveals Germinal Center Associated DNA Primase (GANP) and Other Genes Associated with the Lymphoid Germinal Center Are Regulated by PU.1.
AUTHOR(S): Korade-Mirnics, Zeljka [Reprint Author]; Gao, Yanhua [Reprint Author]; Kawahara, Kazuhiko [Reprint Author]; Sakaguchi, Nabuo [Reprint Author]; Kurosaki, Tomohiro [Reprint Author]; Burnside, Joan [Reprint Author]; Mirnics, Karoly [Reprint Author]; Corey, Seth J. [Reprint Author]
CORPORATE SOURCE: Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, PA, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 336. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

AB Lyn is the only member of the Src family expressed in DT40 avian lymphoma B cells, which provides a unique model to study the singular contribution of this protein tyrosine kinase family to cell signaling. In these cells, gene ablation of Lyn leads to defective B cell receptor (BCR) signaling. cDNA array analysis of Lyn-deficient DT40 B lymphoma cells show that the absence of Lyn leads to downregulation of a small set of genes encoding proteins involved in BCR-signaling, proliferation, control of transcription, immunity/inflammation response and cytoskeletal organization. Most of these expression changes have not been previously associated with Lyn signaling. They include alterations in mRNA levels of GANP, CD74, CD22, NF-kB, EF1a, CD79b, Octamer Binding Factor-1, Ig heavy chain, stathmin, and gamma-actin. Changes in GANP expression were also confirmed in Lyn-deficient mice, suggesting that Lyn has a unique function not compensated for by other Src kinases. As Lyn-deficient mice have impaired development of germinal centers in spleen, the decreased expression of GANP in the Lyn-deficient DT40 cell line and Lyn-deficient mice suggests that Lyn controls the formation and proliferation of germinal centers via GANP. GANP promoter activity was increased in wild-type versus Lyn-deficient cells. Mutation of the PU.1 binding site abrogated activity in wild-type cells and had no effect in Lyn-deficient cells. The presence of Lyn enhanced both PU.1 expression in a northern blot and activity by electrophoretic mobility shift assay. Thus, a new signaling pathway has been described: Lyn fwdarwPU.1fwdarw GANP.

L5 ANSWER 17 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 10
ACCESSION NUMBER: 2001-10470 BIOTECHDS
TITLE: CALPP protein, a polynucleotide encoding it and an antibody; involving vector plasmid pAS2-1-mediated gene transfer for expression in yeast cell
PATENT ASSIGNEE: Sumitomo-Elec.
LOCATION: Japan.
PATENT INFO: JP 2001078779 27 Mar 2001
APPLICATION INFO: JP 1999-263707 17 Sep 1999
PRIORITY INFO: JP 1999-263707 17 Sep 1999
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

OTHER SOURCE: WPI: 2001-313372 [33]
AB A CALPP protein consisting of the disclosed protein sequence, is claimed. Also claimed are: a CALPP protein consisting of a protein sequence in which at least one amino acid is deleted, replaced or added in the sequence; a polynucleotide encoding the protein; an antisense polynucleotide or a derivative of it; and an antibody recognizing the protein; The antibody can be used for the treatment of the detection of autoimmune diseases. In an example, a cDNA encoding CALPP protein was cloned. Thus, yeast two hybrid screening system was used for giving the new protein combining with GANP. Plasmid pAS2-1-Mouse GANP was genetically introduced to Y190 yeast cells and used as the bait. Plasmid pGAD10-mouse new-born cDNA library was used for the screening. The library was screened to give a positive clone. The base sequence of the insert of the plasmid of the positive clone was determined and a DNA primer was prepared from the sequence. A cDNA was isolated by a reverse transcriptase-polymerase chain reaction using B-lymphocyte mRNA as the template. (17pp)

L5 ANSWER 18 OF 22 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001698241 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11641399
TITLE: PU.1 is involved in the regulation of B lineage-associated and developmental stage-dependent expression of the germinal center-associated DNA primase GANP.
AUTHOR: EL-Gazzar M A; Maeda K; Nomiyama H; Nakao M; Kuwahara K; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto, 860-0811 Japan.
SOURCE: The Journal of biological chemistry, (2001 Dec 21) Vol. 276, No. 51, pp. 48000-8. Electronic Publication: 2001-10-18.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ318088
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 18 Dec 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 31 Jan 2002
AB Germinal center-associated DNA primase (GANP) associated with MCM3 of the DNA replication complex is up-regulated selectively in germinal center B cells. We studied promoter activity of the 5' region involved in the developmental stage-dependent expression in B lineage cells by luciferase reporter assay. Selective regulation of ganp expression was observed in the -737-bp promoter region in B and plasma cell lines but was significantly low in pre-B and T cell lines. The deletion constructs displayed a gap decrease after shortening the region from -134 to -108 bp. Further narrowing suggested the involvement of the PU.1 consensus sequence at -126 bp by electrophoretic mobility shift assay. The protein component PU.1 complex is not inhibited with mutated probes at the consensus site but is inhibited with the known PU.1 probe of CD72 and with anti-PU.1 antibody. Moreover, introduction of PU.1 cDNA enhanced the reporter gene activity in a dose-dependent manner in B cells, whereas the reporter construct with the mutated PU.1 site did not respond. Anti-CD40 stimulation induced the reporter activity with a 100% increase, which is not observed with the PU.1-mutated reporter construct. These results demonstrate that the germinal center-associated DNA primase expression is partly regulated by the transcription factor PU.1 expressed in B lineage cells.

L5 ANSWER 19 OF 22 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001492409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11526238
TITLE: Germinal center-associated nuclear protein (GANP) has a phosphorylation-dependent DNA-primase activity that is up-regulated in germinal center regions.
AUTHOR: Kuwahara K; Tomiyasu S; Fujimura S; Nomura K; Xing Y; Nishiyama N; Ogawa M; Imajoh-Ohmi S; Izuta S; Sakaguchi N
CORPORATE SOURCE: Departments of Immunology and Surgery II, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto 860-0811, Japan.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2001 Aug 28) Vol. 98, No. 18, pp. 10279-83.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 6 Sep 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 4 Oct 2001
AB Antigen stimulation induces a rapid proliferation of B cells for expansion of specific B cell clones and their further differentiation into antibody-producing cells in germinal centers of T-dependent antigen-immunized mice. Previously, we identified a 210-kDa germinal center-associated nuclear protein (GANP) that is up-regulated selectively in germinal centers and carries an MCM-binding domain in the carboxyl-terminal side. In addition, here, we found a region (from 414 to 550 aa) in GANP molecule that is slightly similar to the known DNA-primase component p49. The recombinant GANP fragment covering this region synthesizes RNA primers for extension by DNA polymerase I with single-stranded DNA templates in vitro. GANP DNA-primase activity is controlled by phosphorylation at Ser(502) that is induced by CD40-mediated signaling in vitro and in the germinal center B cells stimulated with antigen in vivo. Overexpression of ganp cDNA in Daudi B cells caused the increased DNA synthesis more than the levels of the mock-transfectants. These evidences suggested that the novel DNA-primase GANP is involved in regulation of cell proliferation of antigen-driven B cells in germinal centers.

L5 ANSWER 20 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 13
ACCESSION NUMBER: 2000-14089 BIOTECHDS
TITLE: GANP proteins participating in signal conversion of abnormal B cell differentiation in autoimmune state and having kinase activity, useful in the study of autoimmune mechanisms;
including sense and antisense polynucleotides and an antibody specific to the protein
AUTHOR: Sakaguchi N; Kuwahara K
PATENT ASSIGNEE: Sumitomo-Elec.
LOCATION: Osaka, Japan.
PATENT INFO: WO 2000050611 31 Aug 2000
APPLICATION INFO: WO 1999-JP4634 27 Aug 1999
PRIORITY INFO: JP 99047035 24 Feb 1999
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2000-549411 [50]
AB A GANP protein having a defined 1971 (P1) or 1980 (P2) amino acid sequence is claimed. Also claimed are: a modified GANP protein which has a similar kinase activity as GANP protein which is based on the amino acid sequence of P1 or P2 but with some amino

acids deleted, substituted or/and added; a protein containing the full length amino acid sequence of the GANP protein or modified GANP protein, or a part of them; a polynucleotide encoding any of the proteins; an antisense polynucleotide containing the antisense chain of the base sequence of the polynucleotide; a polynucleotide which has more than or equal to 12 continuous bases of the partial sequence of any of the polynucleotides; a polynucleotide obtained by chemical modification of any of the polynucleotides; and an antibody which can recognise any of the proteins. The proteins are particularly useful in study of autoimmune mechanism. In an example, the cloning of a mouse GANP gene was performed and then the obtained gene was expressed for further studies. (91pp)

L5 ANSWER 21 OF 22 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2000197882 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10733502
TITLE: A novel nuclear phosphoprotein, GANP, is up-regulated in centrocytes of the germinal center and associated with MCM3, a protein essential for DNA replication.
AUTHOR: Kuwahara K; Yoshida M; Kondo E; Sakata A; Watanabe Y; Abe E; Kouno Y; Tomiyasu S; Fujimura S; Tokuhisa T; Kimura H; Ezaki T; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, Kumamoto, Japan.
SOURCE: Blood, (2000 Apr 1) Vol. 95, No. 7, pp. 2321-8. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 5 May 2000
Last Updated on STN: 4 Feb 2003
Entered Medline: 27 Apr 2000

AB Antigen (Ag) immunization induces formation of the germinal center (GC), with large, rapidly proliferating centroblasts in the dark zone, and small, nondividing centrocytes in the light zone. We identified a novel nuclear protein, GANP, that is up-regulated in centrocytes. We found that GANP was up-regulated in GC B cells of Peyer's patches in normal mice and in spleens from Ag-immunized mice. GANP-positive cells appeared in the light zone of the GC, with coexpression of the peanut agglutinin (PNA) (PNA)-positive B220-positive phenotype. The expression of GANP was strikingly correlated with GC formation because Bcl6-deficient mice did not show the up-regulation of GANP. GANP-positive cells were mostly surrounded by follicular dendritic cells. Stimulation with anti-micro and anti-CD40 induced up-regulation of ganp messenger RNA as well as GANP protein in B220-positive B cells in vitro. GANP is a 210-kd protein localized in both the cytoplasm and nuclei, with a homologous region to Map80 that is associated with MCM3, a protein essential for DNA replication. Remarkably, GANP is associated with MCM3 in B cells and MCM3 is also up-regulated in the GC area. These results suggest that the up-regulation of GANP might participate in the development of Ag-driven B cells in GCs through its interaction with MCM3.

L5 ANSWER 22 OF 22 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2001060279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11024281
TITLE: Structure, expression, and chromosomal localization of the human gene encoding a germinal center-associated nuclear protein (GANP) that associates with MCM3 involved in the initiation of DNA

replication.
AUTHOR: Abe E; Kuwahara K; Yoshida M; Suzuki M; Terasaki H; Matsuo Y; Takahashi E I; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, Honjo, 860-0811, Kumamoto, Japan.
SOURCE: Gene, (2000 Sep 19) Vol. 255, No. 2, pp. 219-27.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ010089
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 22 Dec 2000

AB A 210kDa protein named GANP is upregulated in germinal center (GC)-B cells in the spleen of antigen-immunized mouse. We studied a human ganp gene (hganp) encoding a putative polypeptide of 1980 amino acids. The carboxyl-terminal 721-amino-acid sequence of hGANP is identical to Map80, that is presumably generated by alternative splicing of hganp/Map80 gene. The genomic segment carrying hganp and Map80 genes was isolated, and the chromosomal location was determined on 21q22.3. Northern blot analysis with RNAs from various organs demonstrated a single band of 7kb hganp mRNA, which suggests a preferential transcription of hganp gene from the hganp/Map80 locus. The hGANP expression was upregulated in GCs of the tonsil, as demonstrated by in-situ RNA hybridization and immunohistochemical analyses. The hGANP, with the domain (Map-box) capable of binding to MCM3 in B cells, might be involved in regulation of cell-cycle progression and DNA replication of GC-B cells.

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=> d his

     (FILE 'HOME' ENTERED AT 13:13:18 ON 18 JUL 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:13:51 ON 18 JUL 2006
L1           292 S "GANP"
L2            82 S (MOUSE OR MURINE) AND L1
L3       7791094 S CLON? OR EXPRESS? OR RECOMBINANT
L4            70 S L2 AND L3
L5            22 DUP REM L4 (48 DUPLICATES REMOVED)

=> e sakaguchi n/au
E1             2     SAKAGUCHI MUTSUHITO/AU
E2             3     SAKAGUCHI MUTSUO/AU
E3           842 --> SAKAGUCHI N/AU
E4             5     SAKAGUCHI N */AU
E5             1     SAKAGUCHI NABUO/AU
E6            21     SAKAGUCHI NAHOKO/AU
E7             7     SAKAGUCHI NAHOMI/AU
E8             7     SAKAGUCHI NAME NOT TRANSLATED/AU
E9            10     SAKAGUCHI NAO/AU
E10            1     SAKAGUCHI NAOHIRO/AU
E11            1     SAKAGUCHI NAOHISA/AU
E12            7     SAKAGUCHI NAOKI/AU

=> s e3-e5
L6           848 ("SAKAGUCHI N"/AU OR "SAKAGUCHI N *"/AU OR "SAKAGUCHI NABUO"/AU)


=> e kuwahara k/au
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E1            1     KUWAHARA JUNPEI/AU
E2            1     KUWAHARA JUNSHI/AU
E3          893 --> KUWAHARA K/AU
E4           43     KUWAHARA KAIZO/AU
E5            3     KUWAHARA KAIZOU/AU
E6            2     KUWAHARA KANJI/AU
E7            4     KUWAHARA KATSUHIKO/AU
E8            6     KUWAHARA KATSUKI/AU
E9            6     KUWAHARA KATSUMI/AU
E10           1     KUWAHARA KATSUMORI/AU
E11           1     KUWAHARA KATSUNARI/AU
E12          13     KUWAHARA KATSUNORI/AU

=> s e3
L7          893 "KUWAHARA K"/AU

=> d his

     (FILE 'HOME' ENTERED AT 13:13:18 ON 18 JUL 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:13:51 ON 18 JUL 2006
L1           292 S "GANP"
L2            82 S (MOUSE OR MURINE) AND L1
L3       7791094 S CLON? OR EXPRESS? OR RECOMBINANT
L4            70 S L2 AND L3
L5            22 DUP REM L4 (48 DUPLICATES REMOVED)
                 E SAKAGUCHI N/AU
L6           848 S E3-E5
                 E KUWAHARA K/AU
L7           893 S E3

=> s l6 or l7
L8          1637 L6 OR L7

=> s l1 and l8
L9            51 L1 AND L8

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           25 DUP REM L9 (26 DUPLICATES REMOVED)

=> d 1-25 ibib ab

L10  ANSWER 1 OF 25  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN                                    DUPLICATE 1
ACCESSION NUMBER:   2006123954  EMBASE
TITLE:              Increased expression of germinal center-associated nuclear
                    protein (GANP) is associated with malignant
                    transformation of melanocytes.
AUTHOR:             Kageshita T.; Kuwahara K.; Oka M.; Ma D.; Ono T.;
                    Sakaguchi N.
CORPORATE SOURCE:   N. Sakaguchi, Department of Immunology, Graduate School of
                    Medical Sciences, Kumamoto University, 1-1-1 Honjo,
                    Kumamoto 860-8556, Japan. nobusaka@kaiju.medic.kumamoto-
                    u.ac.jp
SOURCE:             Journal of Dermatological Science, (2006) Vol. 42, No. 1,
                    pp. 55-63. .
                    Refs: 19
                    ISSN: 0923-1811  CODEN: JDSCEI
PUBLISHER IDENT.:   S 0923-1811(05)00346-4
COUNTRY:            Ireland
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       013     Dermatology and Venereology
```

016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 2006
Last Updated on STN: 31 Mar 2006

AB Background: Germinal center-associated nuclear protein (GANP) is a newly cloned molecule that is up-regulated in the germinal center B cells. Although GANP functions in the regulation of DNA repair during replication and survival of B cells, little is known about its expression in melanocytic cells. Objectives: To investigate whether GANP and phosphorylated-GANP (P-GANP) are expressed in cultured human melanocytes and melanoma cells and in benign and malignant melanocytic lesions. In addition, we aim to determine whether GANP and P-GANP are associated with malignant transformation of melanocytic lineage. Methods: GANP and P-GANP expression in cultured melanocytic cells was analyzed by immunostaining and in vitro kinase assay. GANP and P-GANP expression in melanocytic lesions was analyzed by immunohistochemistry. Results: GANP and P-GANP were up-regulated in cultured melanoma cells compared to melanocytes. GANP and P-GANP were restricted to nucleus of melanocytes but co-expressed in cytoplasm of melanoma cells. On the other hand, GANP and P-GANP were widely expressed at various levels in melanocytic nevi and melanoma lesions with nuclear and cytoplasmic staining pattern. Melanoma cells showed a stronger intensity of GANP and P-GANP than melanocytic nevus cells, however the staining intensity in primary melanoma lesions was not associated with any clinicopathological variables. Cytoplasmic GANP and P-GANP expression was associated with MCM3 and Ki67 expression. Conclusions: These data suggest, for the first time, that GANP and P-GANP are up-regulated in cultured melanoma cells compared to melanocytes and also they are widely expressed in benign and malignant melanocytic tumor cells.

L10 ANSWER 2 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-22092 BIOTECHDS
TITLE: Novel antibody binding with high affinity to gp120 glycoprotein of HIV, useful for detecting HIV and for treating HIV infection;
involving vector-mediated gene transfer and expression in hybridoma for use in diagnosis and immunotherapy
AUTHOR: SAKAGUCHI N; KUWAHARA K; MINODA C
PATENT ASSIGNEE: KUMAMOTO TECHNOLOGY and IND FOUND
PATENT INFO: WO 2005058963 30 Jun 2005
APPLICATION INFO: WO 2004-JP3046 9 Mar 2004
PRIORITY INFO: JP 2003-418655 16 Dec 2003; JP 2003-418655 16 Dec 2003
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2005-506112 [51]

AB DERWENT ABSTRACT:
NOVELTY - An antibody (I) or its fragment, binding with gp120 glycoprotein of HIV, with a dissociation constant (KD) less than 1.0x10-9(M), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a monoclonal antibody (II) or its fragment with respect to gp120 glycoprotein of HIV with acceptance number FERM BP-08644, is produced by hybridoma cell; (2) a humanized antibody (HA), human antibodies or their fragments, comprising (I) or (II) or variable region of their fragments; (3) a high affinity antibody producing cell, extracted from GANP transgenic non-human mammal or its offspring immunized with antigen

polypeptide containing a fully defined 23 (SEQ ID No: 6) sequences given in the specification; (4) a cell producing monoclonal antibody with respect to gp120 glycoprotein of HIV with acceptance number FERM BP-08644; (5) producing anti-HIV antibody or its fragment; (6) a pharmaceutical composition (PC1) comprising (I) and HA or its fragment; and (7) a kit for detecting HIV, comprising (I) or HA, or their fragments.

BIOTECHNOLOGY - Preferred Antibody: (I) recognizes at least a portion of amino acid sequence of 308-330 of gp120 glycoprotein. (I) has residues 308-330 of SEQ ID No: 6. (I) is a polyclonal or monoclonal antibody.

ACTIVITY - Anti-HIV. No biological data given.

MECHANISM OF ACTION - Immunotherapy.

USE - (I) and HA are useful for detecting HIV. (I) and PC1 are useful for treating HIV infection (claimed).

ADMINISTRATION - PC1 is administered intravenously, subcutaneously, intramuscularly, intraperitoneally, intracutaneously or through abdominal cavity, at a dose of 10 micrograms, preferably 1000-1 ng.

ADVANTAGE - (I) has high binding affinity (KD=1.0x10-9(M)) respective gp120 glycoprotein of HIV.

EXAMPLE - The antibody was produced by standard hybridoma technique using HIV24 N:L43 peptide.(125 pages)

L10 ANSWER 3 OF 25 EMBASE DUPLICATE 2

ACCESSION NUMBER: 2005296152 EMBASE

TITLE: Increased expression of germinal center-associated nuclear protein RNA-primase is associated with lymphomagenesis.

AUTHOR: Fujimura S.; Xing Y.; Takeya M.; Yamashita Y.; Ohshima K.; Kuwahara K.; Sakaguchi N.

CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto 860-8556, Japan.
nobusaka@kaiju.medic.kumamoto-u.ac.jp

SOURCE: Cancer Research, (1 Jul 2005) Vol. 65, No. 13, pp. 5925-5934. .
Refs: 48
ISSN: 0008-5472 CODEN: CNREA8

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
022 Human Genetics
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 5 Aug 2005
Last Updated on STN: 5 Aug 2005

AB Lymphomas arise containing abnormalities of various differentiation stage-specific molecules. In the study reported here, we have shown abnormal up-regulation of germinal center B cell-associated GANP in various human lymphomas including mantle cell, diffuse large B cell, and Hodgkin lymphoma, by immunohistochemical analysis. To study the role of GANP in lymphomagenesis, we generated mutant mice (ganp-Tg) that express the transgenic ganp gene under immunoglobulin enhancer and promoter control. Ganp-Tg mice showed a high incidence of lymphomagenesis (29.5%) after aging with a non-B/non-T cell surface phenotype having slight CD45R/B220 expression and Ig transcripts of rearranged VH-DH-JH IgH loci. Lymphomas generated in ganp-Tg mice displayed similar pathologic characteristics to mouse reticulum cell neoplasm or Hodgkin lymphoma-like lesions. The VH sequences of individual mice showed that the tumors proliferated from a single clone or oligoclones, as is found in human diffuse large B-cell lymphomas and Hodgkin lymphoma. These results suggest that GANP

overexpression is a causative factor in the generation of B lymphomas. .COPYRGT.2005 American Association for Cancer Research.

L10 ANSWER 4 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2005479515 EMBASE
TITLE: Cutting edge: Double-stranded DNA breaks in the IgV region gene were detected at lower frequency in affinity-maturation impeded GANP(-/-) mice.
AUTHOR: Kawatani Y.; Igarashi H.; Matsui T.; Kuwahara K.; Fujimura S.; Okamoto N.; Takagi K.; Sakaguchi N.
CORPORATE SOURCE: Dr. N. Sakaguchi, Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto, 860-8556, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Journal of Immunology, (1 Nov 2005) Vol. 175, No. 9, pp. 5615-5618. .
Refs: 24
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Nov 2005
Last Updated on STN: 17 Nov 2005

AB Double-stranded DNA breaks (DSBs) at the IgV region (IgV) genes might be involved in somatic hypermutation and affinity-maturation of the B cell receptor in response to T cell-dependent Ag. By ligation-mediated PCR, we studied IgV DSBs that occurred in mature germinal center B cells in response to nitrophenyl-chicken γ-globulin in a RAG1-independent, Ag-dependent, and IgV-selective manner. We quantified their levels in GANP-deficient B cells that have impaired generation of high-affinity Ab. GANP(-/-) B cells showed a decreased level of DSBs with blunt ends than control B cells and, on the contrary, the ganp gene transgenic (GANP(Tg)) B cells showed an increased level. These results suggested that the level of IgV DSBs in germinal center B cells is associated with GANP expression, which is presumably required for B cell receptor affinity maturation. Copyright .COPYRGT. 2005 by The American Association of Immunologists, Inc.

L10 ANSWER 5 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4

ACCESSION NUMBER: 2005169954 EMBASE
TITLE: Generation of high-affinity antibody against T cell-dependent antigen in the Ganp gene-transgenic mouse.
AUTHOR: Sakaguchi N.; Kimura T.; Matsushita S.; Fujimura S.; Shibata J.; Araki M.; Sakamoto T.; Minoda C.; Kuwahara K.
CORPORATE SOURCE: Dr. N. Sakaguchi, Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto 860-8556, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Journal of Immunology, (15 Apr 2005) Vol. 174, No. 8, pp. 4485-4494. .
Refs: 35
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 May 2005
Last Updated on STN: 19 May 2005

AB Generation of high-affinity Ab is impaired in mice lacking germinal center-associated DNA primase (GANP) in B cells. In this study, we examined the effect of its overexpression in ganp transgenic C57BL/6 mice (Ganp (Tg)). Ganp(Tg) displayed normal phenotype in B cell development, serum Ig levels, and responses against T cell-independent Ag; however, it generated the Ab with much higher affinity against nitrophenyl-chicken gammaglobulin in comparison with C57BL/6. To further examine the affinity increase, we established hybridomas producing high-affinity mAbs and compared their affinities using BIAcore. C57BL/6 generated high-affinity anti-nitrophenyl mAbs (K(D) .apprx. 2.50 .apprx. 10(-7) M) of IgG1/λ1 and contained the V(H)186.2 region with W33L mutation. Ganp(Tg) generated much higher affinity (K(D) > 1.57 x 10(-9) M) by usage of V(H)186.2 as well as noncanonical V(H)7183 regions. Ganp(Tg) also generated exceptionally high-affinity anti-HIV-1 (V3 peptide) mAbs (K(D) > 9.90 x 10(-11) M) with neutralizing activity. These results demonstrated that GANP is involved in V region alteration generating high-affinity Ab.

L10 ANSWER 6 OF 25 EMBASE DUPLICATE 5
ACCESSION NUMBER: 2005401984 EMBASE
TITLE: Protein phosphatase subunit G5PR is needed for inhibition of B cell receptor-induced apoptosis.
AUTHOR: Xing Y.; Igarashi H.; Wang X.; Sakaguchi N.
CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto 860-8556, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Journal of Experimental Medicine, (5 Sep 2005) Vol. 202, No. 5, pp. 707-719. .
Refs: 74
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Oct 2005
Last Updated on STN: 13 Oct 2005

AB B cell receptor (BCR) cross-linking induces B cell proliferation and sustains survival through the phosphorylation-dependent signals. We report that a loss of the protein phosphatase component G5PR increased the activation-induced cell death (AICD) and thus impaired B cell survival. G5PR associates with GANP, whose expression is up-regulated in mature B cells of the peripheral lymphoid organs. To study G5PR function, the G5pr gene was conditionally targeted with the CD19-Cre combination (G5pr(-/-) mice). The G5pr(-/-) mice had a decreased number of splenic B cells (60% of the controls). G5pr(-/-) B cells showed a normal proliferative response to lipopolysaccharide or anti-CD40 antibody stimulation but not to BCR cross-linking with or without IL-4 in vitro. G5pr(-/-) B cells did not show abnormalities in the BCR-mediated activation of Erks and NF-κB, cyclin D2 induction, or Akt activation. However, G5pr(-/-) B cells were sensitive to AICD caused by BCR cross-linking. This was associated with an increased depolarization of the mitochondrial membrane and the enhanced activation of c-Jun NH(2)-terminal protein kinase and Bim. These results suggest that G5PR is required for the BCR-mediated proliferation associated with the prevention

of AICD in mature B cells. JEM .COPYRGT. The Rockefeller University Press.

L10 ANSWER 7 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-15408 BIOTECHDS
TITLE: Transgenic mammal transformed with germinal center associated nuclear protein (GANP) gene for production of high-affinity antibodies as diagnostic reagents and disease therapy;
involving vector plasmid pLG-mediated gene transfer and expression in host cell for use in therapy
AUTHOR: SAKAGUCHI N
PATENT ASSIGNEE: IMMUNOKICK INC
PATENT INFO: WO 2004040971 21 May 2004
APPLICATION INFO: WO 2003-JP14221 7 Nov 2003
PRIORITY INFO: WO 2002-11598 7 Nov 2002; WO 2002-11598 7 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2004-411378 [38]
AB DERWENT ABSTRACT:
NOVELTY - Transgenic non-human animals and their offspring are new which are transformed with germinal center associated nuclear protein (GANP) gene.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) tissues and organs of the transgenic mammals; (2) preparation of high-affinity antibodies by immunizing the transgenic animals with an antigen; (3) high-affinity antibodies and their fragments obtained by the method; (4) high-affinity antibody secreting cells produced using the method; and (5) drug compositions containing the high-affinity antibodies or their fragments.

BIOTECHNOLOGY - Preferred Mammal: mouse. Preferred antibodies: polyclonal or monoclonal with neutralizing activity at below 10-7M. The antibodies include human or humanized antibodies or their fragments containing V regions from the antibodies prepared using the transgenic animals.

ACTIVITY - Virucide. No suitable data given.

MECHANISM OF ACTION - Viral antigen inhibitor.

USE - Production of high-affinity antibodies to viral antigens for treatment and prevention of infection by viruses such as human immunodeficiency virus and hepatitis C virus.

ADMINISTRATION - Antibody is administered at 1 microgram to 100 mg (preferably 50 microgram to 50 mg) per kilo body weight per day subcutaneous, transdermal, intravenous, intramuscular or intraperitoneal.

EXAMPLE - GANP gene (WO2000/50611) is inserted into pLG vector (a vector containing the enhancer region from human immunoglobulin gene) and used to transform fertilized ova of C57BL/6 mice by microinjection. The transformed ova are implanted and brought to term to give transgenic mice. RT-PCR on total RNA isolated from spleen B cells from these mice shows that GANP has higher expression in these transgenic mice than in wild-type mice. The mice are immunized using 100 microgram of p-nitrophenyl derivatized chicken gamma-globulin (NP-CG). Spleen cells from immunized mice are fused with P3U1 myeloma cells and the hybridomas obtained are screened for anti-NP-CG activity. Supernatant from a culture of positive clone is subjected to ELISA assay using immobilized NP2-BSA or NP17-BSA antigen (bovine serum albumin containing 2 or 17 p-nitrophenyl groups per albumin molecule) and peroxidase-labelled anti-mouse IgG. The ratio of binding to NP2-BSA to that to NP17-BSA is calculated as a measure of neutralizing ability. A similar experiment is conducted using wild-type c57BL/6 mice. The binding ratio for wild-type mice is 30% and for transgenic mice is higher, one hybridoma clone (G2-9) having a binding ratio of 80%.(214 pages)

L10 ANSWER 8 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-15238 BIOTECHDS

TITLE: Transgenic mammals carrying GANP for production of high-affinity antibodies, used as diagnostics and remedies for various diseases e.g. hepatitis C, adult T-cell leukemia, AIDS and mad-cow disease;
plasmid-mediated gene transfer and expression in B-lymphocyte for transplantation in transgenic mouse for recombinant antibody production for use in disease diagnosis

AUTHOR: SAKAGUCHI N

PATENT ASSIGNEE: KUMAMOTO TECHNOLOGY and IND FOUND

PATENT INFO: WO 2004040969 21 May 2004

APPLICATION INFO: WO 2002-JP11598 7 Nov 2002

PRIORITY INFO: WO 2002-11598 7 Nov 2002; WO 2002-11598 7 Nov 2002

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2004-400492 [37]

AB DERWENT ABSTRACT:

NOVELTY - A transgenic mammal is transferred with GANP (undefined) gene, its descendants, or a part of them.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a method for producing a high-affinity antibody by administering an antigen to the transgenic mammal or its descendants prior to obtaining such antibody; (2) a high- affinity antibody or its fragment thus produced; and diagnostics, preventives or remedies for diseases containing the antibodies or their fragments; (3) a human- type antibody or its fragment containing the V region of a high-affinity antibody; (4) remedies containing such human-type antibody; and (5) high-affinity antibody-producing cells collected from the transgenic mammals or their descendants after administering an antigen.

ACTIVITY - Virucide; Cytostatic; Anti-HIV; Neuroprotective. No biological data given.

MECHANISM OF ACTION - None given.

USE - The produced antibodies are useful as diagnostics and remedies for various diseases e.g. hepatitis C, adult T-cell leukemia, AIDS and mad-cow disease.

ADMINISTRATION - Administration of the remedies is oral or non-oral, e.g. at 10 mug/kg to 1000 mg/kg.

ADVANTAGE - Such produced high-affinity antibody is efficacious as diagnostic or remedy.

EXAMPLE - Transgenic mice were obtained after transferring with a mouse GANP gene-containing pLG vector. After administering e.g. trinitrophenyl-keyhole limpet hemocyanin (TNP-KLH) as antigen, the antigen-specific antibody production was verified. (73 pages)

L10 ANSWER 9 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:961842 SCISEARCH

THE GENUINE ARTICLE: 865IC

TITLE: The Sac3 homologue shd1 is involved in mitotic progression in mammalian cells

AUTHOR: Sefat-e-Khuda; Yoshida M; Xing Y; Shimasaki T; Takeya M; Kuwahara K; Sakaguchi N (Reprint)

CORPORATE SOURCE: Kumamoto Univ, Grad Sch Med Sci, Dept Immunol, 1-1-1 Honjo, Kumamoto 8608556, Japan (Reprint); Kumamoto Univ, Grad Sch Med Sci, Dept Immunol, Kumamoto 8608556, Japan; Kumamoto Univ, Grad Sch Med Sci, Dept Cell Pathol, Kumamoto 8608556, Japan; Kumamoto Univ, Inst Resource Dev & Anal, Ctr Resource Anal, Div Isotope Sci, Kumamoto 8600811, Japan; Japan Sci & Technol Agcy, PRESTO, Kawaguchi 3320012, Japan; Japan Sci & Technol Agcy, CREST, Kawaguchi 3320012, Japan
nobusaka@kaiju.medic.kumamoto-u.ac.jp

COUNTRY OF AUTHOR: Japan

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (29 OCT 2004) Vol. 279,

No. 44, pp. 46182-46190.
ISSN: 0021-9258.
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26
ENTRY DATE: Entered STN: 25 Nov 2004
Last Updated on STN: 25 Nov 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Saccharomyces Sac3 required for actin assembly was shown to be involved in DNA replication. Here, we studied the function of a mammalian homologue SHD1 in cell cycle progression. SHD1 is localized on centrosomes at interphase and at spindle poles and mitotic spindles, similar to alpha-tubulin, at M phase. RNA interference suppression of endogenous shd1 caused defects in centrosome duplication and spindle formation displaying cells with a single apparent centrosome and down-regulated Mad2 expression, generating increased micronuclei. Conversely, increased expression of SHD1 by DNA transfection with shd1-green fluorescent protein (gfp) vector for a fusion protein of SHD1 and GFP caused abnormalities in centrosome duplication displaying cells with multiple centrosomes and deregulated spindle assembly with up-regulated Mad2 expression until anaphase, generating polyploidy cells. These results demonstrated that shd1 is involved in cell cycle progression, in particular centrosome duplication and a spindle assembly checkpoint function.

L10 ANSWER 10 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 6
ACCESSION NUMBER: 2004134449 EMBASE
TITLE: Microarray Analysis of Lyn-Deficient B Cells Reveals Germinal Center-Associated Nuclear Protein and Other Genes Associated with the Lymphoid Germinal Center.
AUTHOR: Mirnics Z.K.; Caudell E.; Gao Y.; Kuwahara K.; Sakaguchi N.; Kurosaki T.; Burnside J.; Mirnics K.; Corey S.J.
CORPORATE SOURCE: Dr. S.J. Corey, Division of Pediatrics, Univ. TX-M. D. Anderson Cancer Ctr., 1515 Holcombe Boulevard, Houston, TX 77030, United States. sjcorey@mdanderson.org
SOURCE: Journal of Immunology, (1 Apr 2004) Vol. 172, No. 7, pp. 4133-4141. .
Refs: 57
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 2004
Last Updated on STN: 29 Apr 2004

AB Lyn is the only member of the Src family expressed in DT40 B cells, which provide a unique model to study the singular contribution of this protein tyrosine kinase (PTK) family to cell signaling. In these cells, gene ablation of Lyn leads to defective B cell receptor signaling. Complementary DNA array analysis of Lyn-deficient DT40 cells shows that the absence of Lyn leads to down-regulation of numerous genes encoding proteins involved in B cell receptor signaling, proliferation, control of transcription, immunity/inflammation response, and cytoskeletal organization. Most of these expression changes have not been previously associated with Lyn PTK signaling. They include alterations in mRNA levels of germinal center-associated nuclear protein (germinal center-associated DNA primase) (GANP), CD74, CD22, NF-κB, elongation factor 1α, CD79b, octamer binding factor 1, Ig H chain, stathmin, and γ-actin. Changes in GANP expression were

also confirmed in Lyn-deficient mice, suggesting that Lyn PTK has a unique function not compensated for by other Src kinases. Because Lyn-deficient mice have impaired development of germinal centers in spleen, the decreased expression of GANP in the Lyn-deficient DT40 cell line and Lyn-deficient mice suggests that Lyn controls the formation and proliferation of germinal centers via GANP. GANP promoter activity was higher in wild-type vs Lyn-deficient cells. Mutation of the PU.1 binding site reduced activity in wild-type cells and had no effect in Lyn-deficient cells. The presence of Lyn enhanced PU.1 expression in a Northern blot. Thus, the following new signaling pathway has been described: Lyn→PU.1→ GANP.

L10 ANSWER 11 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 7

ACCESSION NUMBER: 2004057585 EMBASE
TITLE: Germinal center-associated nuclear protein contributes to affinity maturation of B cell antigen receptor in T cell-dependent responses.
AUTHOR: Kuwahara K.; Fujimura S.; Takahashi Y.; Nakagata N.; Takemori T.; Aizawa S.; Sakaguchi N.
CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, Honjo, Kumamoto 860-8556, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (27 Jan 2004) Vol. 101, No. 4, pp. 1010-1015. .
Refs: 50
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 2004
Last Updated on STN: 26 Feb 2004

AB Acquired immunity depends on proliferation and differentiation of antigen (Ag)-specific B cells in germinal centers (GCs) of lymphoid follicles in response to T cell-dependent Ags. Here, we studied the function of GC-associated nuclear protein that is selectively upregulated in GC-B cells. B cell-specific ganp-deficient mice were compromised in affinity maturation of hapten-specific antibodies against T cell-dependent Ags with retarded development of GCs. B cell numbers and development, serum Ig levels, mitogen-induced B cell proliferation in vitro, and responses to T cell-independent Ag were nearly normal; however, the mutant B cells showed a decrease in anti-CD40-induced proliferation and an increased susceptibility to B cell apoptosis in vitro and in vivo. B cell-specific ganp-deficient mice showed a decreased frequency of variable-region somatic mutations, especially of the high-affinity type (W(33) → L) in the V(H)186.2 region against nitrophenyl-chicken gamma globulin, whereas the class switching was normal. We conclude that GC-associated nuclear protein is necessary for generation or maintenance of B cells with high-affinity B cell Ag receptors during the maturation in GCs.

L10 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1164401 HCAPLUS
DOCUMENT NUMBER: 145:25908
TITLE: Critical role of GANP in generation of high-affinity B cells against T cell-dependent antigen
AUTHOR(S): Sakaguchi, N.; Takahashi, Y.; Takemori, T.; Kuwahara, K.
CORPORATE SOURCE: Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

SOURCE: Immunology 2004, [12th International Congress of Immunology and 4th Annual Conference of FOCIS], Montreal, QC, Canada, July 18-23, 2004 (2004), E718C5035/1-E718C5035/6. Monduzzi Editore: Bologna, Italy.
CODEN: 69HJYL; ISBN: 88-7587-070-5
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English

AB Acquired immunity is dependent on generation of high-affinity B cells against the T cell dependent (TD)-antigens (Ags) during the proliferation and differentiation in germinal center (GC) of peripheral lymphoid organs. The primary repertoire of virgin B cells provides a necessary but limited source of Ag-reactive B cells, but they further differentiate into high-affinity B cells during immune responses. To elucidate the mol. mechanism of generation of high-affinity B cells, we studied GC-associated nuclear protein (GANP) that appeared up-regulated in GC-B cells upon immunization with TD-Ags. Conditional targeting of ganp in B cells displayed impairment of generation of high-affinity B cells upon immunization with nitrophenyl chicken γ-globulin (NP-CG). The low-affinity in the ganp-deficient B cells is manifested in lack of the mutation at 33W to L of VH186.2 with λ1 light chain. The data suggested the new notion regarding mechanism in Ig diversification in peripheral lymphoid tissues.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 25 EMBASE DUPLICATE 8
ACCESSION NUMBER: 2003228381 EMBASE
TITLE: Spontaneous increase of plasma-like cells with high GANP expression in the extrafollicular region of lymphoid organs of autoimmune-prone mice.
AUTHOR: Fujimura S.; Kuwahara K.; Ezaki T.; Tomita K.; Hirose S.; Sakaguchi N.
CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Kumamoto Univ. School of Medicine, 2-2-1, Honjo, Kumamoto 860-0811, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Journal of Autoimmunity, (2003) Vol. 20, No. 4, pp. 291-301. .
Refs: 32
ISSN: 0896-8411 CODEN: JOAUEP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2003
Last Updated on STN: 26 Jun 2003

AB Autoimmune-prone mice bear a hyper-active B cell population generated spontaneously in peripheral lymphoid organs. Expression of β RNA-primase GANP was shown to be an activation marker in lymphoid follicle germinal center (GC) B cells after immunization with T cell-dependent antigen (TD-Ag) in normal mice. In this study, we examined the expression of GANP in lymphoid tissues of autoimmune-prone mice. GANP expression was up-regulated in GC-B cells after stimulation with TD-Ags; however, highly GANP-positive (GANP(hi)) cells were also observed in lymph nodes of non-immunized MRL/lpr mice. GANP(hi)cells in lymph nodes as well as in spleens of the different autoimmune-prone strains, MRL/lpr, NZB, (NZBxNZW)F1 and BXSB, gradually increased with age. This population was detected only in small numbers in the red pulp region of the spleen after immunization with TD-Ag in normal C57BL/6 and BALB/c mice. GANP (hi)cells had a B220(-)IgM(+)Syndecan-1(+)phenotype, but were negative for

PAS-staining and bromo-deoxyuridine incorporation. These results demonstrate that GANP(hi)plasma-like cells appear in lymph nodes of autoimmune mice during aging, suggesting that the new plasma cell population might be generated after hyper-activation of B cells during the course of autoimmune disease. .COPYRGT. 2003 Elsevier Science Ltd. All rights reserved.

L10 ANSWER 14 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:505664 SCISEARCH
THE GENUINE ARTICLE: 669TR
TITLE: Critical role of GANP in B cell activation following T cell-dependent antigens
AUTHOR: Sakaguchi N (Reprint); Kuwahara K; Fujimura S; Takahashi Y; Takemori T
CORPORATE SOURCE: Kumamoto Univ, Sch Med, Dept Immunol, CREST, JST, Kumamoto 8600811, Japan; Kumamoto Univ, Sch Med, Dept Immunol, PRESTO, JST, Kumamoto 8600811, Japan; Natl Inst Infect Dis, Dept Immunol, Tokyo, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: FASEB JOURNAL, (14 APR 2003) Vol. 17, No. 7, Supp. [S], pp. C190-C190.
ISSN: 0892-6638.
PUBLISHER: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 3 Jul 2003
Last Updated on STN: 3 Jul 2003

L10 ANSWER 15 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 9

ACCESSION NUMBER: 2002306373 EMBASE
TITLE: MCM3-binding GANP DNA-primase is associated with a novel phosphatase component G5PR.
AUTHOR: Kono Y.; Maeda K.; Kuwahara K.; Yamamoto H.; Miyamoto E.; Yonezawa K.; Takagi K.; Sakaguchi N.
CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Kumamoto Univ. School of Medicine, 2-2-1 Honjo, Kumamoto 860-0811, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Genes to Cells, (2002) Vol. 7, No. 8, pp. 821-834. .
Refs: 45
ISSN: 1356-9597 CODEN: GECEFL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 13 Sep 2002

AB Background: GANP, carrying DNA-primase and MCM3-binding domains, is up-regulated in germinal centre B cells. To understand the regulatory function of GANP upon MCM complex, we searched for GANP -associated molecules by yeast two-hybrid screening. Results: Using the 1 kb fragment (G5) of the ganp cDNA, we identified a clone named G5PR that is structurally homologous to known regulatory subunits of protein phosphatases (PPases) and determined the association of G5PR with GANP in vivo in the DNA transfectant. G5PR is associated with protein phosphatase 5 (PP5) through its tetratricopeptide-repeat (TPR) domain. Pull-down assays demonstrated that G5PR is also associated with protein phosphatase 2A (PP2A), the complex of A subunit (PR65) and the catalytic (C) subunit (PP2Ac), similar to the B" subunit. The G5PR-associated complex had phosphatase activity on casein, histone H1 and

MCM3 in vitro, but the addition of G5PR did not stimulate or inhibit the phosphatase activities of PP5 and PP2A. The cellular localization of G5PR in transfected cells varies during cell cycling, appearing in the nucleus during prophase, in the peri-chromatin during mitotic phase, and in the cytoplasm after cell division. Conclusion: G5PR is capable of recruiting two kinds of PPases, PP5 and PP2A, into the GANP/MCM3 complex, which might regulate its phosphorylation state during cell cycle progression.

L10 ANSWER 16 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:313378 SCISEARCH
THE GENUINE ARTICLE: 533MG
TITLE: Identification of a phosphatase G5PR bound with GC-B cell associated DNA-primase GANP, interacting with MCM3 involved in DNA-replication
AUTHOR: Maeda K (Reprint); Kono Y; Kuwahara K; Sakaguchi N
CORPORATE SOURCE: Kumamoto Univ, Sch Med, Kumamoto 8600811, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: FASEB JOURNAL, (20 MAR 2002) Vol. 16, No. 4, Part 1, pp. A348-A348.
ISSN: 0892-6638.
PUBLISHER: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 26 Apr 2002
Last Updated on STN: 26 Apr 2002

L10 ANSWER 17 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003300776 EMBASE
TITLE: Involvement of GANP in B cell activation in T cell-dependent antigen response.
AUTHOR: Sakaguchi N.; Fujimura S.; Kuwahara K.
CORPORATE SOURCE: N. Sakaguchi, Department of Immunology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto 860-0811, Japan. nobusaka@kaiju.medic.kumamoto-u.ac.jp
SOURCE: Developmental Immunology, (2002) Vol. 9, No. 3, pp. 169-172. .
Refs: 13
ISSN: 1044-6672 CODEN: DEIME7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Aug 2003
Last Updated on STN: 10 Aug 2003

AB Adaptive immunity is dependent on proliferation of antigen-driven B cells for clonal expansion in germinal centers (GCs) against T cell-dependent antigens (TD-Ag), accompanied with somatic hypermutation of variable-region gene and class switching of B cell antigen receptors. To study molecular mechanisms for B cell differentiation in GCs, we have identified and studied a 210kDa GANP protein expressed in GC-B cells. GANP has domains for MCM3-binding and RNA-primase activities and is selectively up-regulated in centrocytes surrounded with follicular dendritic cells (FDCs) upon immunization with TD-Ag in vivo and in B cells stimulated with anti-CD40 monoclonal antibody in vitro, which suggested that GANP plays a certain important role in the

maturation of immunoglobulin or selection of B cells in GC during the immune response to TD-Ag. Since this up-regulation has not been detected in T cells in GCs and in Concanavalin A-stimulated T cells in vitro, selective function of GANP molecule on B cell proliferation and differentiation might exist.

L10 ANSWER 18 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:572919 SCISEARCH
THE GENUINE ARTICLE: 614JK
TITLE: Microarray analysis of Lyn-deficient B cells reveals germinal center associated DNA primase (GANP) and other genes associated with the lymphoid germinal center are regulated by PU.1.
AUTHOR: Korade-Mirnics Z (Reprint); Gao Y H; Kawahara K; Sakaguchi N; Kurosaki T; Burnside J; Mirnics K; Corey S J
CORPORATE SOURCE: Childrens Hosp Pittsburgh, Pittsburgh, PA 15213 USA; Kumamoto Univ, Sch Med, Kumamoto 860, Japan; Kansai Med Univ, Kansai, Japan; Univ Delaware, Inst Biotechnol, Newark, DE 19716 USA; Univ Pittsburgh, Pittsburgh, PA 15260 USA; Univ Texas, MD Anderson Canc Ctr, Houston, TX 77030 USA
COUNTRY OF AUTHOR: USA; Japan
SOURCE: BLOOD, (16 NOV 2002) Vol. 100, No. 11, Part 1, pp. 91A-92A. MA 336.
ISSN: 0006-4971.
PUBLISHER: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 25 Jul 2003
Last Updated on STN: 25 Jul 2003

L10 ANSWER 19 OF 25 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:356436 BIOSIS
DOCUMENT NUMBER: PREV200300356436
TITLE: Microarray Analysis of Lyn-Deficient B Cells Reveals Germinal Center Associated DNA Primase (GANP) and Other Genes Associated with the Lymphoid Germinal Center Are Regulated by PU.1.
AUTHOR(S): Korade-Mirnics, Zeljka [Reprint Author]; Gao, Yanhua [Reprint Author]; Kawahara, Kazuhiko [Reprint Author]; Sakaguchi, Nabuo [Reprint Author]; Kurosaki, Tomohiro [Reprint Author]; Burnside, Joan [Reprint Author]; Mirnics, Karoly [Reprint Author]; Corey, Seth J. [Reprint Author]
CORPORATE SOURCE: Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, PA, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 336. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

AB Lyn is the only member of the Src family expressed in DT40 avian lymphoma

B cells, which provides a unique model to study the singular contribution of this protein tyrosine kinase family to cell signaling. In these cells, gene ablation of Lyn leads to defective B cell receptor (BCR) signaling. cDNA array analysis of Lyn-deficient DT40 B lymphoma cells show that the absence of Lyn leads to downregulation of a small set of genes encoding proteins involved in BCR-signaling, proliferation, control of transcription, immunity/inflammation response and cytoskeletal organization. Most of these expression changes have not been previously associated with Lyn signaling. They include alterations in mRNA levels of GANP, CD74, CD22, NF-kB, EF1a, CD79b, Octamer Binding Factor-1, Ig heavy chain, stathmin, and gamma-actin. Changes in GANP expression were also confirmed in Lyn-deficient mice, suggesting that Lyn has a unique function not compensated for by other Src kinases. As Lyn-deficient mice have impaired development of germinal centers in spleen, the decreased expression of GANP in the Lyn-deficient DT40 cell line and Lyn-deficient mice suggests that Lyn controls the formation and proliferation of germinal centers via GANP. GANP promoter activity was increased in wild-type versus Lyn-deficient cells. Mutation of the PU.1 binding site abrogated activity in wild-type cells and had no effect in Lyn-deficient cells. The presence of Lyn enhanced both PU.1 expression in a northern blot and activity by electrophoretic mobility shift assay. Thus, a new signaling pathway has been described: Lyn fwdarwPU.1fwdarw GANP.

L10 ANSWER 20 OF 25 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001698241 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11641399
TITLE: PU.1 is involved in the regulation of B lineage-associated and developmental stage-dependent expression of the germinal center-associated DNA primase GANP.
AUTHOR: EL-Gazzar M A; Maeda K; Nomiyama H; Nakao M; Kuwahara K; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto, 860-0811 Japan.
SOURCE: The Journal of biological chemistry, (2001 Dec 21) Vol. 276, No. 51, pp. 48000-8. Electronic Publication: 2001-10-18.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ318088
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 18 Dec 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 31 Jan 2002

AB Germinal center-associated DNA primase (GANP) associated with MCM3 of the DNA replication complex is up-regulated selectively in germinal center B cells. We studied promoter activity of the 5' region involved in the developmental stage-dependent expression in B lineage cells by luciferase reporter assay. Selective regulation of ganp expression was observed in the -737-bp promoter region in B and plasma cell lines but was significantly low in pre-B and T cell lines. The deletion constructs displayed a gap decrease after shortening the region from -134 to -108 bp. Further narrowing suggested the involvement of the PU.1 consensus sequence at -126 bp by electrophoretic mobility shift assay. The protein component PU.1 complex is not inhibited with mutated probes at the consensus site but is inhibited with the known PU.1 probe of CD72 and with anti-PU.1 antibody. Moreover, introduction of PU.1 cDNA enhanced the reporter gene activity in a dose-dependent manner in B cells, whereas the reporter construct with the mutated PU.1 site did not respond. Anti-CD40 stimulation induced the reporter activity with a 100% increase, which is not observed with the PU.1-mutated reporter construct. These

results demonstrate that the germinal center-associated DNA primase expression is partly regulated by the transcription factor PU.1 expressed in B lineage cells.

L10 ANSWER 21 OF 25 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001492409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11526238
TITLE: Germinal center-associated nuclear protein (GANP) has a phosphorylation-dependent DNA-primase activity that is up-regulated in germinal center regions.
AUTHOR: Kuwahara K; Tomiyasu S; Fujimura S; Nomura K; Xing Y; Nishiyama N; Ogawa M; Imajoh-Ohmi S; Izuta S; Sakaguchi N
CORPORATE SOURCE: Departments of Immunology and Surgery II, Kumamoto University School of Medicine, 2-2-1, Honjo, Kumamoto 860-0811, Japan.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2001 Aug 28) Vol. 98, No. 18, pp. 10279-83.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 6 Sep 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 4 Oct 2001

AB Antigen stimulation induces a rapid proliferation of B cells for expansion of specific B cell clones and their further differentiation into antibody-producing cells in germinal centers of T-dependent antigen-immunized mice. Previously, we identified a 210-kDa germinal center-associated nuclear protein (GANP) that is up-regulated selectively in germinal centers and carries an MCM-binding domain in the carboxyl-terminal side. In addition, here, we found a region (from 414 to 550 aa) in GANP molecule that is slightly similar to the known DNA-primase component p49. The recombinant GANP fragment covering this region synthesizes RNA primers for extension by DNA polymerase I with single-stranded DNA templates in vitro. GANP DNA-primase activity is controlled by phosphorylation at Ser(502) that is induced by CD40-mediated signaling in vitro and in the germinal center B cells stimulated with antigen in vivo. Overexpression of ganp cDNA in Daudi B cells caused the increased DNA synthesis more than the levels of the mock-transfectants. These evidences suggested that the novel DNA-primase GANP is involved in regulation of cell proliferation of antigen-driven B cells in germinal centers.

L10 ANSWER 22 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:41422 SCISEARCH
THE GENUINE ARTICLE: 496AL
TITLE: B cell-stage dependent transcription regulation of GC-associated DNA primase GANP
AUTHOR: El-Gazzar M A (Reprint); Maeda K; Kuwahara K; Nomiyama H; Nakao M; Sakaguchi N
CORPORATE SOURCE: Kumamoto Univ, Sch Med, Dept Immunol, Kumamoto 8600811, Japan; Kumamoto Univ, Sch Med, Kumamoto 860, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (NOV 2001) Vol. 12, Supp. [S], pp. 354A-354A. MA 1944.
ISSN: 1059-1524.
PUBLISHER: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
DOCUMENT TYPE: Conference; Journal

LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 18 Jan 2002
Last Updated on STN: 18 Jan 2002

L10 ANSWER 23 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2000-14089 BIOTECHDS
TITLE: GANP proteins participating in signal conversion of abnormal B cell differentiation in autoimmune state and having kinase activity, useful in the study of autoimmune mechanisms;
including sense and antisense polynucleotides and an antibody specific to the protein
AUTHOR: Sakaguchi N; Kuwahara K
PATENT ASSIGNEE: Sumitomo-Elec.
LOCATION: Osaka, Japan.
PATENT INFO: WO 2000050611 31 Aug 2000
APPLICATION INFO: WO 1999-JP4634 27 Aug 1999
PRIORITY INFO: JP 99047035 24 Feb 1999
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2000-549411 [50]
AB A GANP protein having a defined 1971 (P1) or 1980 (P2) amino acid sequence is claimed. Also claimed are: a modified GANP protein which has a similar kinase activity as GANP protein which is based on the amino acid sequence of P1 or P2 but with some amino acids deleted, substituted or/and added; a protein containing the full length amino acid sequence of the GANP protein or modified GANP protein, or a part of them; a polynucleotide encoding any of the proteins; an antisense polynucleotide containing the antisense chain of the base sequence of the polynucleotide; a polynucleotide which has more than or equal to 12 continuous bases of the partial sequence of any of the polynucleotides; a polynucleotide obtained by chemical modification of any of the polynucleotides; and an antibody which can recognise any of the proteins. The proteins are particularly useful in study of autoimmune mechanism. In an example, the cloning of a mouse GANP gene was performed and then the obtained gene was expressed for further studies. (91pp)

L10 ANSWER 24 OF 25 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2000197882 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10733502
TITLE: A novel nuclear phosphoprotein, GANP, is up-regulated in centrocytes of the germinal center and associated with MCM3, a protein essential for DNA replication.
AUTHOR: Kuwahara K; Yoshida M; Kondo E; Sakata A; Watanabe Y; Abe E; Kouno Y; Tomiyasu S; Fujimura S; Tokuhisa T; Kimura H; Ezaki T; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, Kumamoto, Japan.
SOURCE: Blood, (2000 Apr 1) Vol. 95, No. 7, pp. 2321-8.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 5 May 2000
Last Updated on STN: 4 Feb 2003
Entered Medline: 27 Apr 2000
AB Antigen (Ag) immunization induces formation of the germinal center (GC), with large, rapidly proliferating centroblasts in the dark zone, and small, nondividing centrocytes in the light zone. We identified a novel

nuclear protein, GANP, that is up-regulated in centrocytes. We found that GANP was up-regulated in GC B cells of Peyer's patches in normal mice and in spleens from Ag-immunized mice. GANP-positive cells appeared in the light zone of the GC, with coexpression of the peanut agglutinin (PNA) (PNA)-positive B220-positive phenotype. The expression of GANP was strikingly correlated with GC formation because Bcl6-deficient mice did not show the up-regulation of GANP. GANP-positive cells were mostly surrounded by follicular dendritic cells. Stimulation with anti-micro and anti-CD40 induced up-regulation of ganp messenger RNA as well as GANP protein in B220-positive B cells in vitro. GANP is a 210-kd protein localized in both the cytoplasm and nuclei, with a homologous region to Map80 that is associated with MCM3, a protein essential for DNA replication. Remarkably, GANP is associated with MCM3 in B cells and MCM3 is also up-regulated in the GC area. These results suggest that the up-regulation of GANP might participate in the development of Ag-driven B cells in GCs through its interaction with MCM3.

L10 ANSWER 25 OF 25 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2001060279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11024281
TITLE: Structure, expression, and chromosomal localization of the human gene encoding a germinal center-associated nuclear protein (GANP) that associates with MCM3 involved in the initiation of DNA replication.
AUTHOR: Abe E; Kuwahara K; Yoshida M; Suzuki M; Terasaki H; Matsuo Y; Takahashi E I; Sakaguchi N
CORPORATE SOURCE: Department of Immunology, Kumamoto University School of Medicine, Honjo, 860-0811, Kumamoto, Japan.
SOURCE: Gene, (2000 Sep 19) Vol. 255, No. 2, pp. 219-27. Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ010089
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 4 Feb 2003
Entered Medline: 22 Dec 2000
AB A 210kDa protein named GANP is upregulated in germinal center (GC)-B cells in the spleen of antigen-immunized mouse. We studied a human ganp gene (hganp) encoding a putative polypeptide of 1980 amino acids. The carboxyl-terminal 721-amino-acid sequence of hGANP is identical to Map80, that is presumably generated by alternative splicing of hganp/Map80 gene. The genomic segment carrying hganp and Map80 genes was isolated, and the chromosomal location was determined on 21q22.3. Northern blot analysis with RNAs from various organs demonstrated a single band of 7kb hganp mRNA, which suggests a preferential transcription of hganp gene from the hganp/Map80 locus. The hGANP expression was upregulated in GCs of the tonsil, as demonstrated by in-situ RNA hybridization and immunohistochemical analyses. The hGANP, with the domain (Map-box) capable of binding to MCM3 in B cells, might be involved in regulation of cell-cycle progression and DNA replication of GC-B cells.

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(FILE 'HOME' ENTERED AT 13:13:18 ON 18 JUL 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 13:13:51 ON 18 JUL 2006
L1 292 S "GANP"

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L2            82 S (MOUSE OR MURINE) AND L1
L3       7791094 S CLON? OR EXPRESS? OR RECOMBINANT
L4            70 S L2 AND L3
L5            22 DUP REM L4 (48 DUPLICATES REMOVED)
                 E SAKAGUCHI N/AU
L6           848 S E3-E5
                 E KUWAHARA K/AU
L7           893 S E3
L8          1637 S L6 OR L7
L9            51 S L1 AND L8
L10           25 DUP REM L9 (26 DUPLICATES REMOVED)
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	Issue Date	Pages	Document ID	Title
1	20060316	52	US 20060057695 A1	GANP protein
2	20060223	52	US 20060040372 A1	GANP protein
3	20041118	52	US 20040229309 A1	GANP protein
4	20040226	621	US 20040038292 A1	Wound healing biomarkers
5	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
6	20030227	122	US 20030040089 A1	Protein-protein interactions in adipocyte cells
7	20050913	50	US 6943237 B2	GANP protein
8	20041130	50	US 6825020 B1	GANP protein
9	20040316	434	US 6706867 B1	DNA array sequence selection
10	20040106	50	US 6673913 B1	GANP proteins

	Issue Date	Pages	Document ID	Title
1	20060316	52	US 20060057695 A1	GANP protein
2	20060223	52	US 20060040372 A1	GANP protein
3	20050203	23	US 20050023555 A1	GaN-based field effect transistor
4	20041118	52	US 20040229309 A1	GANP protein
5	20040226	621	US 20040038292 A1	Wound healing biomarkers
6	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
7	20030227	122	US 20030040089 A1	Protein-protein interactions in adipocyte cells
8	20060502	22	US 7038253 B2	GaN-based field effect transistor of a normally-off type
9	20051108	156	US 6962989 B1	Corynebacterium glutamicum genes encoding novel proteins
10	20050913	50	US 6943237 B2	GANP protein
11	20041130	50	US 6825020 B1	GANP protein
12	20040316	434	US 6706867 B1	DNA array sequence selection
13	20040106	50	US 6673913 B1	GANP proteins

	Issue Date	Pages	Document ID	Title
1	20060316	52	US 20060057695 A1	GANP protein
2	20060223	52	US 20060040372 A1	GANP protein
3	20041118	52	US 20040229309 A1	GANP protein
4	20050913	50	US 6943237 B2	GANP protein
5	20041130	50	US 6825020 B1	GANP protein
6	20040106	50	US 6673913 B1	GANP proteins

	L #	Hits	Search Text
1	L1	98	"GANP"
2	L2	737911	kinase$2
3	L3	10	l1 same l2
4	L4	864833	clon$3 or express$3 or recombinant
5	L5	13	l1 same l4
6	L6	9851	SAKAGUCHI KUWAHARA
7	L7	6	l1 and l6